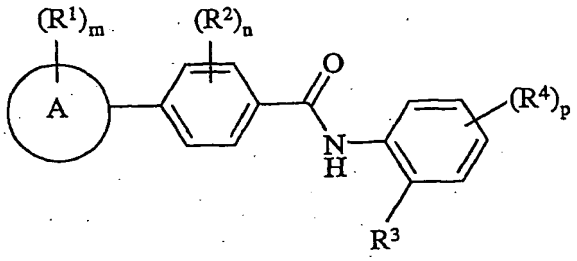
Claims

1. A compound of the formula (I):



(I)

wherein:

Ring A is a heterocyclyl, wherein if said heterocyclyl contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from K;

R^1 is a substituent on carbon and is selected from halo, nitro, cyano, hydroxy, trifluoromethyl, trifluoromethoxy, amino, carboxy, carbamoyl, mercapto, sulphamoyl, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}alkoxy, C_{1-6}alkanoyl, C_{1-6}alkanoyloxy, *N*-(C_{1-6}alkyl)amino, *N,N*-(C_{1-6}alkyl)$_2$amino, C_{1-6}alkanoylamino, *N*-(C_{1-6}alkyl)carbamoyl, *N,N*-(C_{1-6}alkyl)$_2$carbamoyl, C_{1-6}alkylS(O)$_a$ wherein a is 0 to 2, C_{1-6}alkoxycarbonyl, *N*-(C_{1-6}alkyl)sulphamoyl, *N,N*-(C_{1-6}alkyl)$_2$sulphamoyl, aryl, aryloxy, arylC_{1-6}alkyl, heterocyclic group, (heterocyclic group)C_{1-6}alkyl, or a group (B-E-); wherein R^1, including group (B-E-), may be optionally substituted on carbon by one or more W; and wherein if said heterocyclic group contains an -NH- moiety that nitrogen may be optionally substituted by J;

W is halo, nitro, cyano, hydroxy, trifluoromethyl, trifluoromethoxy, amino, carboxy, carbamoyl, mercapto, sulphamoyl, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}alkoxy, C_{1-6}alkanoyl, C_{1-6}alkanoyloxy, *N*-(C_{1-6}alkyl)amino, *N,N*-(C_{1-6}alkyl)$_2$amino, C_{1-6}alkanoylamino, *N*-(C_{1-6}alkyl)carbamoyl, *N,N*-(C_{1-6}alkyl)$_2$carbamoyl, C_{1-6}alkylS(O)$_a$ wherein a is 0 to 2, C_{1-6}alkoxycarbonyl, *N*-(C_{1-6}alkyl)sulphamoyl, *N,N*-(C_{1-6}alkyl)$_2$sulphamoyl, or a group (B'-E'-); wherein W, including group (B'-E'-), may be optionally substituted on carbon by one or more Y;

Y and Z are independently selected from halo, nitro, cyano, hydroxy, trifluoromethyl, trifluoromethoxy, amino, carboxy, carbamoyl, mercapto, sulphamoyl, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}alkoxy, C_{1-6}alkanoyl, C_{1-6}alkanoyloxy, *N*-(C_{1-6}alkyl)amino, *N,N*-(C_{1-6}alkyl)$_2$amino, C_{1-6}alkanoylamino, *N*-(C_{1-6}alkyl)carbamoyl,

N,*N*-(C_{1-6}alkyl)$_2$carbamoyl, C_{1-6}alkylS(O)$_a$ wherein a is 0 to 2, C_{1-6}alkoxycarbonyl, *N*-(C_{1-6}alkyl)sulphamoyl or *N*,*N*-(C_{1-6}alkyl)$_2$sulphamoyl;

G, J and K are independently selected from C_{1-8}alkyl, C_{2-8}alkenyl, C_{1-8}alkanoyl, C_{1-8}alkylsulphonyl, C_{1-8}alkoxycarbonyl, carbamoyl, *N*-(C_{1-8}alkyl)carbamoyl, *N*,*N*-(C_{1-8}alkyl)carbamoyl, benzyloxycarbonyl, benzoyl, phenylsulphonyl, aryl, arylC_{1-6}alkyl or (heterocyclic group)C_{1-6}alkyl; wherein G, J and K may be optionally substituted on carbon by one or more Q; and wherein if said heterocyclic group contains an -NH- moiety that nitrogen may be optionally substituted by hydrogen or C_{1-6}alkyl;

Q is halo, nitro, cyano, hydroxy, trifluoromethyl, trifluoromethoxy, amino, carboxy, carbamoyl, mercapto, sulphamoyl, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}alkoxy, C_{1-6}alkanoyl, C_{1-6}alkanoyloxy, *N*-(C_{1-6}alkyl)amino, *N*,*N*-(C_{1-6}alkyl)$_2$amino, C_{1-6}alkanoylamino, *N*-(C_{1-6}alkyl)carbamoyl, *N*,*N*-(C_{1-6}alkyl)$_2$carbamoyl, C_{1-6}alkylS(O)$_a$ wherein a is 0 to 2, C_{1-6}alkoxycarbonyl, C_{1-6}alkoxycarbonylamino, *N*-(C_{1-6}alkyl)sulphamoyl, *N*,*N*-(C_{1-6}alkyl)$_2$sulphamoyl, aryl, aryloxy, aryl C_{1-6}alkyl, arylC_{1-6}alkoxy, heterocyclic group, (heterocyclic group)C_{1-6}alkyl, (heterocyclic group)C_{1-6}alkoxy, or a group (B"-E"-); wherein Q, including group (B"-E"-), may be optionally substituted on carbon by one or more Z;

B, B' and B" are independently selected from C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, C_{3-8}cycloalkylC_{1-6}alkyl, aryl, arylC_{1-6}alkyl, heterocyclic group, (heterocyclic group)C_{1-6}alkyl, phenyl or phenylC_{1-6}alkyl; wherein B, B' and B" may be optionally substituted on carbon by one or more D; and wherein if said heterocyclic group contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from G;

E, E' and E" are independently selected from -N(R^a)-, -O-, -C(O)O-, -OC(O)-, -C(O)-, -N(R^a)C(O)-, -N(R^a)C(O)N(R^b)-, -N(R^a)C(O)O-, -OC(O)N(R^a)-, -C(O)N(R^a)-, -S(O)$_r$-, -SO_2N(R^a)-, -N(R^a)SO_2-; wherein R^a and R^b are independently selected from hydrogen or C_{1-6}alkyl optionally substituted by one or more F and r is 0-2;

D and F are independently selected from halo, nitro, cyano, hydroxy, trifluoromethyl, trifluoromethoxy, amino, carboxy, carbamoyl, mercapto, sulphamoyl, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}alkoxy, C_{1-6}alkanoyl, C_{1-6}alkanoyloxy, *N*-(C_{1-6}alkyl)amino, *N*,*N*-(C_{1-6}alkyl)$_2$amino, C_{1-6}alkanoylamino, *N*-(C_{1-6}alkyl)carbamoyl, *N*,*N*-(C_{1-6}alkyl)$_2$carbamoyl, C_{1-6}alkylS(O)$_a$ wherein a is 0 to 2, C_{1-6}alkoxycarbonyl, *N*-(C_{1-6}alkyl)sulphamoyl or *N*,*N*-(C_{1-6}alkyl)$_2$sulphamoyl;

m is 0, 1, 2, 3 or 4; wherein the values of R^1 may be the same or different;

R^2 is halo;

n is 0, 1 or 2; wherein the values of R^2 may be the same or different;

R^3 is amino or hydroxy;

R^4 is halo, nitro, cyano, hydroxy, trifluoromethyl, trifluoromethoxy, amino, carboxy, carbamoyl, mercapto, sulphamoyl, C_{1-3}alkyl, C_{2-3}alkenyl, C_{2-3}alkynyl, C_{1-3}alkoxy, C_{1-3}alkanoyl, C_{1-3}alkanoyloxy, *N*-(C_{1-3}alkyl)amino, *N,N*-(C_{1-3}alkyl)$_2$amino, C_{1-3}alkanoylamino, *N*-(C_{1-3}alkyl)carbamoyl, *N,N*-(C_{1-3}alkyl)$_2$carbamoyl, C_{1-3}alkylS(O)$_a$ wherein a is 0 to 2, C_{1-3}alkoxycarbonyl, *N*-(C_{1-3}alkyl)sulphamoyl, *N,N*-(C_{1-3}alkyl)$_2$sulphamoyl;

p is 0, 1 or 2; wherein the values of R^4 may be the same or different;

or a pharmaceutically acceptable salt or *in vivo* hydrolysable ester or amide thereof;

with the proviso that said compound is not

N-(2-amino-6-hydroxyphenyl)-4-(1-methylhomopiperazin-4-yl)benzamide;

N-(2-amino-6-methylphenyl)-4-(1-methylhomopiperazin-4-yl)benzamide;

N-(2-aminophenyl)-4-(1-*t*-butoxycarbonylhomopiperazin-4-yl)benzamide; or

N-(2-aminophenyl)-4-(1-methylhomopiperazin-4-yl)benzamide.

2. A compound of the formula (I) according to claim 1wherein:

Ring A is a pyridyl, quinolyl, indolyl, pyrimidinyl, morpholinyl, piperidinyl, piperazinyl, pyradazinyl, pyrazinyl, thiazolyl, thienyl, thienopyrimidinyl, thienopyridinyl, purinyl, triazinyl, oxazolyl, pyrazolyl, or furanyl; wherein if Ring A contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from K.

3. A compound of the formula (I) according to claim 1 wherein:

R^1 is a substituent on carbon and is selected from halo, amino, C_{1-6}alkyl, C_{1-6}alkoxy, *N*-(C_{1-6}alkyl)amino, aryl, aryloxy, arylC_{1-6}alkyl, heterocyclic group, (heterocyclic group)C_{1-6}alkyl, or a group (B-E-); wherein R^1, including group (B-E-), may be optionally substituted on carbon by one or more W; and wherein if said heterocyclic group contains an -NH- moiety that nitrogen may be optionally substituted by J;

W is hydroxy, mercapto, C_{1-6}alkyl, C_{1-6}alkoxy, *N,N*-(C_{1-6}alkyl)$_2$amino or a group (B'-E'-); wherein W, including group (B'-E'-), may be optionally substituted on carbon by one or more Y;

Y and Z are independently selected from halo, nitro, cyano, hydroxy, C_{1-6}alkoxy, *N,N*-(C_{1-6}alkyl)$_2$amino or C_{1-6}alkanoylamino;

G, J and K are independently selected from C_{1-8}alkyl, C_{2-8}alkenyl, C_{1-8}alkanoyl, aryl, arylC_{1-6}alkyl or (heterocyclic group)C_{1-6}alkyl; wherein G, J and K may be optionally substituted on carbon by one or more Q; and wherein if said heterocyclic group contains an -NH- moiety that nitrogen may be optionally substituted by hydrogen or C_{1-6}alkyl;

Q is cyano, hydroxy, C_{1-6}alkoxy, C_{1-6}alkanoyloxy, C_{1-6}alkoxycarbonyl, C_{1-6}alkoxycarbonylamino, aryl, aryloxy or a group (B"-E"-); wherein Q, including group (B"-E"-), may be optionally substituted on carbon by one or more Z;

B, B' and B" are independently selected from C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, C_{3-8}cycloalkylC_{1-6}alkyl, aryl, arylC_{1-6}alkyl, heterocyclic group, (heterocyclic group)C_{1-6}alkyl, phenyl or phenylC_{1-6}alkyl; wherein B, B' and B" may be optionally substituted on carbon by one or more D; and wherein if said heterocyclic group contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from G;

E, E' and E" are independently selected from $-N(R^a)-$, -O-, -C(O)O-, -OC(O)-, -C(O)-, $-N(R^a)C(O)-$, $-N(R^a)C(O)N(R^b)-$, $-N(R^a)C(O)O-$, $-OC(O)N(R^a)-$, $-C(O)N(R^a)-$, $-S(O)_r-$, $-SO_2N(R^a)-$, $-N(R^a)SO_2-$; wherein R^a and R^b are independently selected from hydrogen or C_{1-6}alkyl optionally substituted by one or more F and r is 0-2;

D and F are independently selected from halo, C_{1-6}alkoxy or *N,N*-(C_{1-6}alkyl)$_2$amino.

4. A compound of the formula (I) according to claim 1 wherein m is 1.

5. A compound of the formula (I) according to claim 1 wherein R^2 is fluoro and n is 0 or 1.

6. A compound of the formula (I) according to claim 1 wherein R^3 is amino.

7. A compound of the formula (I) according to claim 1 wherein p is 0.

8. A compound of formula (I) according to claim 1 wherein:

Ring A is a pyridyl, quinolyl, indolyl, pyrimidinyl, morpholinyl, piperidinyl, piperazinyl, pyradazinyl, pyrazinyl, thiazolyl, thienyl, thienopyrimidinyl, thienopyridinyl, purinyl, triazinyl, oxazolyl, pyrazolyl, or furanyl; wherein if Ring A contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from K;

R^1 is a substituent on carbon and is selected from halo, amino, C_{1-6}alkyl, C_{1-6}alkoxy, *N*-(C_{1-6}alkyl)amino, aryl, aryloxy, arylC_{1-6}alkyl, heterocyclic group, (heterocyclic group)C_{1-6}alkyl, or a group (B-E-); wherein R^1, including group (B-E-), may be optionally substituted on carbon by one or more W; and wherein if said heterocyclic group contains an -NH- moiety that nitrogen may be optionally substituted by J;

W is hydroxy, mercapto, C_{1-6}alkyl, C_{1-6}alkoxy, *N,N*-(C_{1-6}alkyl)$_2$amino or a group (B'-E'-); wherein W, including group (B'-E'-), may be optionally substituted on carbon by one or more Y;

Y and Z are independently selected from halo, nitro, cyano, hydroxy, C_{1-6}alkoxy, *N,N*-(C_{1-6}alkyl)$_2$amino or C_{1-6}alkanoylamino;

G, J and K are independently selected from C_{1-8}alkyl, C_{2-8}alkenyl, C_{1-8}alkanoyl, aryl, arylC_{1-6}alkyl or (heterocyclic group)C_{1-6}alkyl; wherein G, J and K may be optionally substituted on carbon by one or more Q; and wherein if said heterocyclic group contains an -NH- moiety that nitrogen may be optionally substituted by hydrogen or C_{1-6}alkyl;

Q is cyano, hydroxy, C_{1-6}alkoxy, C_{1-6}alkanoyloxy, C_{1-6}alkoxycarbonyl, C_{1-6}alkoxycarbonylamino, aryl, aryloxy or a group (B"-E"-); wherein Q, including group (B"-E"-), may be optionally substituted on carbon by one or more Z;

B, B' and B" are independently selected from C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-8}cycloalkyl, C_{3-8}cycloalkylC_{1-6}alkyl, aryl, arylC_{1-6}alkyl, heterocyclic group, (heterocyclic group)C_{1-6}alkyl, phenyl or phenylC_{1-6}alkyl; wherein B, B' and B'' may be optionally substituted on carbon by one or more D; and wherein if said heterocyclic group contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from G;

E, E' and E" are independently selected from -N(R^a)-, -O-, -C(O)O-, -OC(O)-, -C(O)-, -N(R^a)C(O)-, -N(R^a)C(O)N(R^a)-, -N(R^a)C(O)O -, -OC(O)N(R^a)-, -C(O)N(R^a)-, -S(O)$_r$-, -SO_2N(R^a)-, -N(R^a)SO_2-; wherein R^a and R^b are independently selected from hydrogen or C_{1-6}alkyl optionally substituted by one or more F and r is 0-2;

D and F are independently selected from halo, C_{1-6}alkoxy or *N,N*-(C_{1-6}alkyl)$_2$amino;

m is 0, 1, 2, 3 or 4; wherein the values of R^1 may be the same or different;

R^2 is fluoro or chloro;

n is 0, 1 or 2, wherein the values of R^2 may be the same or different;

R^3 is amino or hydroxy;

R^4 is halo, nitro, cyano, hydroxy, trifluoromethyl, trifluoromethoxy, amino, carboxy or carbamoyl;

p is 0, 1 or 2, wherein the values of R^4 may be the same or different;

or a pharmaceutically acceptable salt or *in vivo* hydrolysable ester or amide thereof.

9. A compound of formula (I) according to claim 1 wherein:

Ring A is pyridin-4-yl, pyridin-3-yl, pyridin-2-yl, quinolin-8-yl, pyrimidin-6-yl, pyrimidin-5-yl, pyrimidin-4-yl, morpholin-4-yl, piperidin-4-yl, piperidin-3-yl, piperdin-2-yl, piperazin-4-yl, pyridazin-5-yl, pyrazin-6-yl, thiazol-2-yl, thien-2-yl, thieno[3,2d]pyrimidinyl, thieno[3,2b]pyrimidinyl, thieno[3,2b]pyridinyl, purin-6-yl or triazin-6-yl; wherein if Ring A contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from K;

R^1 is a substituent on carbon and is selected from fluoro, chloro, amino, methyl, ethyl, propyl, methoxy, *N*-methylamino, *N*-ethylamino, *N*-propylamino, *N*-butylamino, phenyl, naphthylethyl, piperazin-1-yl, piperidin-1-yl, piperidin-4-yl, 2-(thiomethyl)-pyrimidin-4-yl, tetrahydrofuran-2-ylmethyl, tetrahydropyran-2-ylmethyl, 1,2,5-thiadiazol-3-ylethyl, piperidin-1-ylmethyl, pyridin-2-ylmethyl, or a group (B-E-); wherein R^1, including group (B-E-), may be optionally substituted on carbon by one or more W; and wherein if said heterocyclic group contains an -NH- moiety that nitrogen may be optionally substituted by J;

W is hydroxy, methyl, ethyl, ethoxy, *N,N*-(diethyl)amino, *N,N*-(dibutyl)amino, or a group (B'-E'-); wherein W, including group (B'-E'-), may be optionally substituted on carbon by one or more Y;

Y and Z are independently selected from fluoro, chloro, bromo, nitro, cyano, hydroxy, methoxy, *N,N*-(dimethyl)amino or methylcarbonylamino;

G, J and K are independently selected from methyl, ethyl, propyl, pentyl, 2-methylbutyl, butyl, acetyl, benzyl, 3-(pyrrol-1-yl)propyl or pyrrolidin-2-one-(5*S*)-methyl; wherein G, J and K may be optionally substituted on carbon by one or more Q; and wherein if said heterocyclic group contains an -NH- moiety that nitrogen may be optionally substituted by hydrogen or methyl;

Q is cyano, hydroxy, methoxy, ethoxy, methylcarbonyloxy, methoxycarbonyl, *t*-butoxycarbonylamino, phenyl or a group (B"-E"-); wherein Q, including group (B"-E"-), may be optionally substituted on carbon by one or more Z;

B, B' and B" are independently selected from methyl, ethyl, propyl, cyclohexyl, phenyl, benzyl, 1,2,3,4-tetrahydroquinolinyl, 3-morpholinopropyl, 2-morpholinoethyl, 2-pyrrolidin-1-ylethyl, 3-morpholinopropyl, 3-(4-methylpiperazin-1-yl)propyl, 2-piperidin-1-

ylethyl, 3-piperidin-1-ylpropyl, pyridin-3-ylmethyl or imidazol-1-ylpropyl; wherein B, B' and B'' may be optionally substituted on carbon by one or more D; and wherein if said heterocyclic group contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from G;

E, E' and E'' are independently selected from -N(R^a)-, -O-, -C(O)-, -NHC(O)-, -N(R^a)C(O)O-; wherein R^a is hydrogen or methyl optionally substituted by one or more F;

D and F are independently selected from fluoro, methoxy or ethoxy;

m is 0, 1, or 2; wherein the values of R^1 may be the same or different;

R^2 is fluoro;

n is 0 or 1;

R^3 is amino;

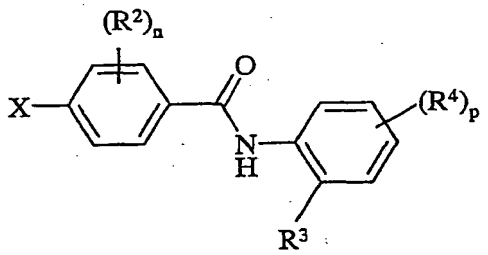
R^4 is halo;

p is 0, 1 or 2, wherein the values of R^4 may be the same or different;

or a pharmaceutically acceptable salt or *in vivo* hydrolysable ester or amide thereof.

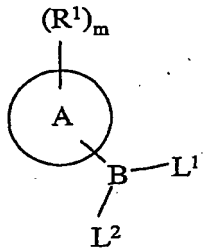
10. A process for preparing a compound of formula (I) or a pharmaceutically acceptable salt or an *in vivo* hydrolysable ester thereof, according to claim 1, which process comprises of:

(a) the reaction of a compound of the formula (II)



(II)

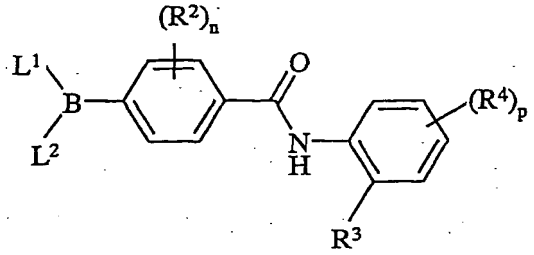
wherein X is a reactive group, with a compound of the formula (III)



(III)

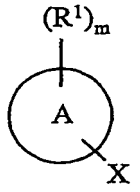
wherein L^1 and L^2 are ligands;

(b) the reaction of a compound of the formula **(IV)**



(IV)

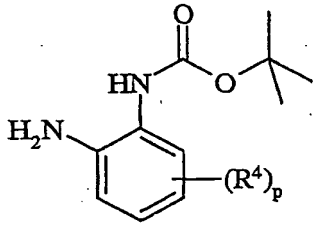
wherein L^1 and L^2 are ligands, with a compound of the formula **(V)**



(V)

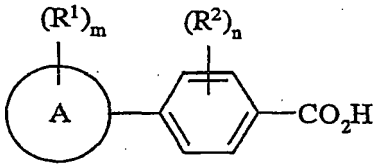
wherein X is a reactive group; or

(c) the reaction, in the presence of 4-(4,6-dimethoxy-1,3,5-triazinyl-2-yl)-4-methylmorpholinium chloride, of a compound of the formula **(VI)**



(VI)

with a compound of the formula **(VII)**



(VII)

and thereafter if necessary:

i) converting a compound of the formula **(I)** into another compound of the formula **(I)**; and/or

ii) removing any protecting groups.

11. A pharmaceutical composition which comprises a compound of the formula (I), or a pharmaceutically acceptable salt or *in vivo* hydrolysable ester or amide thereof, according to claims 1 to 9 in association with a pharmaceutically-acceptable diluent or carrier.

12. A compound of the formula (I), or a pharmaceutically acceptable salt or *in vivo* hydrolysable ester or amide thereof, according to claims 1 to 9 for use as a medicament.

13. The use of a compound of the formula (I), or a pharmaceutically acceptable salt or *in vivo* hydrolysable ester or amide thereof, according to claims 1 to 9 in the manufacture of a medicament for use in the production of a HDAC inhibitory effect in a warm-blooded animal such as man.

14. A method for producing a HDAC inhibitory effect in a warm-blooded animal, such as man, in need of such treatment which comprises administering to said animal an effective amount of a compound of the formula (I), or a pharmaceutically acceptable salt or *in vivo* hydrolysable ester or amide thereof, according to claims 1 to 9.

15. The use of a compound of the formula (I), or a pharmaceutically acceptable salt or *in vivo* hydrolysable ester or amide thereof, according to claims 1 to 9 in the manufacture of a medicament for use in the treatment of cancer.

16. A method of treating cancer in a warm-blooded animal, such as man, in need of such treatment which comprises administering to said animal an effective amount of a compound of the formula (I), or a pharmaceutically acceptable salt or *in vivo* hydrolysable ester or amide thereof, according to claims 1 to 9.

17. The use of a compound of the formula (I), or a pharmaceutically acceptable salt or *in vivo* hydrolysable ester or amide thereof, according to claims 1 to 9 for use in the treatment of cancer.